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## Formulation and evaluation of osmotic drug delivery system of ibuprofen.

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### Special Article Artículo Especial

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### RESUMEN

**Objetivos:** El objetivo del presente trabajo ha sido formular y evaluar el sistema de suministro de ibuprofeno mediante bomba osmótica para proporcionar una concentración uniforme de fármaco en el sitio de absorción y por lo tanto mantener la concentración plasmática dentro del intervalo terapéutico, lo que minimiza los efectos secundarios y reduce la frecuencia de administración.

**Material y Métodos:** En el presente trabajo, 5 formulaciones (F1 a F5) de sistemas de administración de ibuprofeno osmótico (odds) se prepararon utilizando dos osmoagentes (NaCl y KCl) en dos concentraciones y un control (F6) (sin osmoagentes) por la técnica de granulación en húmedo. Los excipientes utilizados en este estudio no alteran las propiedades fisicoquímicas del fármaco, según lo testado por FTIR. Antes de la compresión, los gránulos preparados se evaluaron para la fluidez y la compresión. Después de la compresión, los comprimidos se evaluaron para la dureza, espesor, variación de peso, la friabilidad, el porcentaje de ganancia de peso, contenido de fármaco, la liberación *in vitro* y estudios de estabilidad.

**Resultados:** Los resultados revelaron que los parámetros pre y post-compresión están dentro de los límites. Entre todas las formulaciones, F3 mostró una liberación controlada de fármacos de 63,54% al final de la décima hora. Los resultados de formulación optimizada (F3) sometido a estudios de estabilidad durante 60 días a  $27^{\circ} \pm 2^{\circ}\text{C}/60 \pm 5\% \text{HR}$  y  $50 \pm 2^{\circ}\text{C}/75 \pm 5\% \text{HR}$  mostraron que no hubo ningún cambio significativo en el contenido de fármaco y el porcentaje de liberación del fármaco y el producto fue estable incluso después de 2 meses.

**Conclusiones:** En el estudio, se llegó a la conclusión de que la tableta de bomba osmótica ibuprofeno preparado con cloruro de potasio (10%) como osmoagente y acetato de celulosa como el polímero de revestimiento puede ser considerado como una alternativa adecuada actualmente disponibles para la formulaciones de ibuprofeno.

**PALABRAS CLAVE:** Granulación húmeda, Ibuprofeno, Osmoagente, Sistema osmótico de liberación de fármacos.

### ABSTRACT

**Aim:** The present work was aimed to formulate and evaluate osmotic pump delivery system of Ibuprofen to provide a uniform concentration of drug at the absorption site and thereby maintain the plasma concentration within therapeutic range, which minimizes side effects and reduces the frequency of administration.

**Material and Methods:** In the present work, 5 formulations (F<sub>1</sub> to F<sub>5</sub>) of Ibuprofen osmotic drug delivery systems (ODDS) were prepared using two osmogens (NaCl and KCl) in two concentrations and a control F<sub>6</sub> (without osmogens) by wet granulation technique. The excipients used in this study did not alter physicochemical properties of the drug, as tested by FTIR. Prior to compression, the prepared granules were evaluated for flow and compression characteristics. After compression, the tablets were evaluated for hardness, thickness, weight variation, friability, percentage of weight gain, drug content, *in vitro* release and stability studies.

**Results:** The results revealed that the pre-compression and post-compression parameters are within the limits. Among all the formulations, F<sub>3</sub> showed a controlled drug release of 63.54% at the end of 10<sup>th</sup> hour. The results of optimized formulation (F<sub>3</sub>) subjected to stability studies for 60 days at  $27^{\circ} \pm 2^{\circ}\text{C}/60 \pm 5\% \text{RH}$  and  $50^{\circ} \pm 2^{\circ}\text{C}/75 \pm 5\% \text{RH}$  showed that there was no significant change in the drug content and percentage drug release and the product was stable even after 2 months.

**Conclusions:** From the study, it was concluded that Ibuprofen osmotic pump tablet prepared with potassium chloride (10%) as osmogent and cellulose acetate as coating polymer may be considered as a suitable alternative to currently available formulations of Ibuprofen.

**KEY WORDS:** Ibuprofen, Osmogent, Osmotic drug delivery system, Wet granulation.

## INTRODUCTION

Controlled release delivery system provides a uniform concentration of drug at the absorption site and thus after absorption allow maintenance of plasma concentration within a therapeutic range. Among controlled-release devices, osmotically driven systems hold a prominent place because of their reliability and ability to deliver the contents at predetermined zero-order rates for prolonged periods.<sup>1</sup> Osmotically controlled oral drug delivery system utilizes the principle of osmotic pressure for the controlled delivery of active agent.<sup>2</sup> An osmotic system releases a therapeutic agent at a predetermined, zero order delivery rate based on the principle of Osmosis, which is movement of a solvent from lower concentration of solute towards higher concentration of solute across a semi-permeable membrane. After administration of osmotic system, water is imbibed into the core osmotically through semi-permeable membrane resulting in development of hydrostatic pressure that pumps drug containing solution or suspensions out of the core through one or more delivery ports. The delivery from the system is controlled by the water influx through semi-permeable membrane.<sup>3</sup> one of the most rate controlling factor that must be optimized is the osmotic pressure gradient between inside the compartment and the external environment. The rate of drug release mainly depends upon the osmotic pressure created by osmogens. The simplest and most predictable way to achieve a constant osmotic pressure for constant delivery of drug is to maintain a saturated solution of suitable osmotic agent in the compartment. Osmotic pump tablet (OPT) generally consists of a core including the drug, an osmotic agent, other excipients and semi-permeable membrane coat.<sup>4</sup> Ibuprofen is a Non-steroidal Anti-inflammatory analgesic agent. It has a relatively short biological half-life of 2-4 hours, thereby requiring twice daily dosing in large number of patients.<sup>5,6,7</sup> Because of its short biological half-life and hazards of adverse gastrointestinal (GI) reactions, the development of oral sustained-release formulations of this drug is highly desirable, in order to achieve improved therapeutic efficacy and patient compliance.<sup>8,9</sup> The present work was aimed to formulate and evaluate an osmotic pump delivery system of Ibuprofen by the pores formed in-situ and thereby avoiding laser drilling of tablets and risk of orifice blocking.

## MATERIALS AND METHODS

### Materials:

Ibuprofen was obtained from Sun Pharmaceuticals, Chennai, India. Cellulose acetate, Magnesium stearate and Talc were supplied by Loba Chemie Pvt. Ltd, Mumbai, India. Polyethylene glycol 400 was purchased from Paxmy

Speciality Chemicals, Chennai, India. Dicalcium phosphate was obtained from Finar Chemicals Ltd, Ahmedabad, Sodium chloride from Molychem, Mumbai, Potassium chloride from Reachem Laboratory Chemicals Pvt. Ltd, Chennai, Polyvinyl pyrrolidone from Yarrow Chem. Products, Mumbai, Sodium hydroxide from Thomas Baker Chemicals Pvt. Ltd, Mumbai, India. Potassium Dihydrogen Phosphate and Isopropyl Alcohol were procured from S.D. Fine Chem. Pvt. Ltd, Mumbai, India. All other solvents and reagents used were of analytical grade.

### Methods:

#### Method of preparation of ibuprofen core tablets

Ibuprofen core tablets were prepared by using wet granulation method. Five formulations were developed by using two different osmogens separately and in combination with varying proportions of other ingredients as shown in Table-1. The sixth formulation was developed as control (without osmogens).

Ibuprofen and all other ingredients were passed through sieve#60 separately. The drug and other excipients were triturated in the mortar. PVP K<sub>30</sub> was dissolved in isopropyl alcohol (IPA). This solvent mixture was added to the powder mixture little by little until coherent mass was formed. The coherent mass was kept at room temperature for air drying (until IPA smell ceases/ evaporated) and then passed through sieve#10. Granules were dried in a hot air oven at 50°C for two hours.<sup>10</sup> The dried granules were passed through sieve#20, mixed with Talc and Magnesium stearate and then the granules were compressed into tablets with approximately 5-6 kg/cm<sup>2</sup> hardness using 10 station Mini Press tablet compression machine.

#### Coating of tablets

The core tablets were coated by using 5% w/w of cellulose acetate (CA) and plasticizer, polyethylene glycol 400 (15% v/v with respect to cellulose acetate).<sup>11</sup> Both CA and PEG 400 were dissolved in 50 ml of acetone and methanol mixture in ratio of 4:1. The coating operation was performed in a conventional laboratory model stainless steel spray coating pan with hot air blower. The speed of the pan was adjusted to 30 rpm. The inlet air temperature was 40-45°C and the coating was done manually by intermittent spraying and drying technique (4 ml/minute). Coated tablets were allowed to dry completely in a hot air oven at 60°C for 12 hours. The weight of the tablet and thickness was determined before and after coating<sup>12</sup>.

#### Drug-excipient interaction studies

To determine any interaction between drug and excipients, Fourier Transform Infra red (FT-IR) study was carried out.

FT-IR analysis of pure drug, individual osmogen and combination of drug and osmogens in highest concentration were taken for the study. Samples were compressed with potassium chloride and transformed into disk. Disk was applied to the centre of the sample holding device and scanned between 4000-400  $\text{cm}^{-1}$  in a SHIMADZU FT-IR (IR Affinity -1) spectrophotometer.<sup>13</sup>

#### Evaluation of granules

The prepared granules were evaluated for pre-compression parameters such as Angle of repose, Bulk density, Tapped density, Compressibility index and Hausner's ratio. The angle of repose was determined by fixed cone method. The bulk density and tapped density were determined by bulk density apparatus.<sup>14</sup>

The compressibility index was determined by Carr's compressibility index and the Hausner's ratio was calculated by using the formula:

$$\text{Carr's index (\%)} = [(TD-BD) / TD] \times 100.$$

$$\text{Hausner's Ratio} = \text{Tapped density} / \text{Bulk density}.$$

$$TD = \text{Tapped density, } BD = \text{bulk density}.$$

#### Evaluation of tablets

After compression, Ibuprofen osmotic tablets both uncoated and coated were evaluated for their thickness, hardness, weight variation, Percentage weight gain and content uniformity. Friability of uncoated osmotic tablets was determined.

#### Thickness and hardness

The thickness of the tablets was measured by using Vernier Caliper scale.<sup>15</sup> Hardness is the force required to break a tablet in diametric compression. Hardness of the tablets was determined by Monsanto hardness tester.<sup>1</sup>

#### Weight variation

Twenty tablets were selected at random and average weight was determined. Then individual tablets were weighed and the individual weight was compared with the average weight.<sup>17</sup> Not more than two of the individual weights deviate from the official standard limit.

#### Friability

Friability is a tablet property that evaluates the ability of the tablet to withstand abrasion in packaging, handling and shipping. Friability was measured by Roche Friabilator. The tablets that lose less than 1.0% of their weight are generally acceptable.<sup>18</sup>

$$\text{Percentage friability} = \frac{(\text{Initial weight} - \text{Final weight})}{\text{Initial weight}} \times 100.$$

#### Percentage weight gain

Twenty tablets (before and after coating) from each formulation were selected randomly, weighed individually and average weight was calculated. The average weight increase due to coating was determined from the difference in weight of coated and uncoated tablets.

$$\text{Percentage Weight gain} = \frac{(\text{Weight gain} / \text{Initial weight before coating})}{\text{Initial weight before coating}} \times 100.$$

#### Drug content analysis

Five tablets were taken and powdered. From the powder, amount equivalent to 100mg of Ibuprofen was weighed accurately and dissolved in pH 7.2 buffer solution. The solution was suitably diluted and the drug content was determined by measuring the absorbance at 221nm using UV-Visible spectrophotometer.<sup>19</sup> The analytical method for drug (Ibuprofen) content determination was referred and taken from Indian Pharmacopoeia. The Analytical method was validated as per ICH guidelines in terms of Accuracy, Precision, Reproducibility, Selectivity, Limit of quantification, Linearity. The standards method validation data were found to be adequate and sufficient and met the laboratory method requirements.

#### In vitro drug release studies

*In vitro* drug release of the formulations was carried out in a USP dissolution apparatus (paddle type) at a rotating speed of 50 rpm and temperature of  $37^{\circ} \pm 0.5^{\circ}\text{C}$ . One tablet was placed in each jar. The dissolution medium used was 900 ml of phosphate buffer pH 7.2. Samples of 10 ml were withdrawn at specified time intervals (every 1 hour) over 10 hour period and the medium was replenished with fresh 10 ml dissolution fluid.<sup>20</sup> The withdrawn samples after suitable dilution were analyzed spectrophotometrically at 221 nm and the drug release was calculated.

#### Drug release kinetics:

To determine the release kinetics, data obtained from *in vitro* drug release studies were tested with the following mathematical model such as Zero order equation, first order equation, Higuchi square root law and Korsmeyer-Peppas equation.<sup>21</sup>

#### Stability studies

The best formulation was selected for the stability study and the samples were packed in air tight containers and stored in stability chamber maintained at  $27^{\circ} \pm 2^{\circ}\text{C} / 60 \pm$

**Table 1. Composition of Ibuprofen core tablets**

INGREDIENTS(mg)	FORMULATION CODE					
	F <sub>1</sub>	F <sub>2</sub>	F <sub>3</sub>	F <sub>4</sub>	F <sub>5</sub>	F <sub>6</sub>
Ibuprofen	200	200	200	200	200	200
Sodium Chloride	50	100	-	-	50	-
Potassium Chloride	-	-	50	100	50	-
Polyvinyl Pyrrolidone K <sub>30</sub>	10	10	10	10	10	10
Iso Propyl Alcohol	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Dicalcium Phosphate	228	178	228	178	178	278
Magnesium Stearate	4	4	4	4	4	4
Talc	8	8	8	8	8	8

Weight of each tablet = 500 mg

5% RH and 50 $\pm$ 2 $^{\circ}$ C/75  $\pm$  5% RH for two months.<sup>22</sup> The samples were withdrawn on 31<sup>st</sup>, 46<sup>th</sup> and 61<sup>st</sup> days and evaluated for the appearance, drug content and in-vitro drug release studies.

## RESULTS and DISCUSSION

In the present work, five formulations (F<sub>1</sub> to F<sub>5</sub>) of Ibuprofen osmotic drug delivery systems (ODDS) were developed by using two different osmogens. The sixth formulation (F<sub>6</sub>) was developed as control (without osmogens). The tablets were prepared by wet granulation method. The composition of Ibuprofen core tablets were showed in Table 1.

The IR studies of pure Ibuprofen, Ibuprofen with higher proportion of sodium chloride (20%w/w), Ibuprofen with potassium chloride (20%w/w) and Ibuprofen with sodium chloride (20%w/w) and potassium chloride (20%w/w) were carried out. Osmogens such as sodium chloride, potassium chloride are transparent to infrared radiation. Therefore no signals appeared for sodium chloride and potassium chloride. But IR spectrum of pure Ibuprofen, Ibuprofen + sodium chloride, Ibuprofen + potassium chloride and Ibuprofen + sodium chloride + potassium chloride were similar fundamental peaks and pattern which revealed that there were no significant interactions between the drug and osmogens. IR spectroscopic studies indicated that the drug is compatible with the osmogens.

The granules flow property can be assessed from Angle of repose, Carr's Compressibility Index and Hausner's ratio. The angle of repose of all the formulations was between 29 $^{\circ}$ -33 $^{\circ}$ . It proved that the flow properties of all formulations are good. The bulk density, tapped density, Compressibility index and Hausner ratio are within the acceptable limits. It indicates that the granules showed good flow character. The results are shown in Table 2.

The thickness of the coated tablets was ranging between 4.81 and 4.95 mm whereas the thickness of uncoated tablets

was ranged between 3.06 and 3.20 mm. The thickness of coated tablets was greater than that of the uncoated tablets to the extent of 1.63 - 1.89 mm. The variation may be due to coating and the difference gives thickness of the coating (semi permeable) membrane. The thickness of ibuprofen tablets are presented in Table 3.

The hardness of the coated tablets ranged from 6.2 - 6.5 kg/cm<sup>2</sup> when compared to uncoated tablets whose hardness ranges from 5.1 - 5.6 kg/cm<sup>2</sup>. The increase in the hardness may be due to increased thickness and intact coating membrane. The friability of formulated tablets ranged between 0.04 and 0.09 %, that it is within the compendia limits, which showed that the tablets possess good mechanical strength. The results are presented in Table 4.

The weight of one tablet is 500 mg. As per USP 24 - NF 19, if the average weight of Tablet is more than 324mg the acceptable deviation is  $\pm$ 5%. The deviation of individual weight from the average weight of tablets were within  $\pm$ 5%. The result of weight variation test showed that the weight of all formulated uncoated tablets was within 496.51-499.52 mg. Hence the tablets passed the weight variation test. The percentage weight increase after coating was found to be between 3.209 and 4.232 which may be desirable to withstand the hydrostatic pressure created by the osmogen (Table 5).

The Ibuprofen content for coated as well as uncoated tablets should be within 95-105% as per the specification given in British pharmacopoeia. The percentage of the drug content was more than 96 % and less than 98%. So it was within the limit as per B.P. Hence the drug content in the coated as well as uncoated tablets was found to be within the prescribed limits ( $\pm$  5% w/w of Ibuprofen). The results are presented in Table 6.

The percentage of drug released from Ibuprofen osmotic drug delivery system coated with cellulose acetate membrane was investigated. The cumulative percentage drug release of osmotic pump controlled Ibuprofen tablet using 10 % and 20 % sodium chloride as osmogens (F<sub>1</sub> and F<sub>2</sub>) was 65.08 % and 67.15 % respectively after ten hours. Similarly the cumulative percentage of drug release using potassium chloride was 63.54 % and 66.87 % respectively in ten hours (F<sub>3</sub> and F<sub>4</sub>). The *in vitro* results showed that the release pattern was slightly increased in the formulations containing higher concentration of osmogen sodium chloride compared to Potassium chloride. In formulation F<sub>5</sub> combination of two osmogens (10 % sodium chloride and 10 % potassium chloride) were used, they gave increased percentage of drug release (69.74 %) in ten hours. The increased percentage of drug release showed by formulation F<sub>5</sub> may be due to increased level of hydrating

**Table 2. Evaluation of Ibuprofen Granules**

PARAMETERS	FORMULATION CODE					
	F <sub>1</sub>	F <sub>2</sub>	F <sub>3</sub>	F <sub>4</sub>	F <sub>5</sub>	F <sub>6</sub>
Angle of Repose( $\theta$ )*	29.58±0.53	33.23±0.35	30.96±0.19	31.26±0.60	29.35±0.48	31.05±0.25
Bulk Density (gm/cm <sup>3</sup> )*	0.35±0.02	0.31±0.03	0.37±0.01	0.38±0.07	0.35±0.10	0.41±0.06
Tapped Density (gm/cm <sup>3</sup> )*	0.40±0.01	0.35±0.05	0.42±0.06	0.40±0.08	0.44±0.06	0.46±0.01
Compressibility Index (%)*	11.73±0.79	12.10±0.54	13.63±0.38	11.57±1.05	12.60±0.86	12.98±0.65
Hausner's Ratio*	1.12±0.15	1.13±0.28	1.13±0.12	1.14±0.85	1.12±0.74	1.13±0.24

\*All values are expressed as mean  $\pm$  standard deviation (SD) n=3

**Table 3. Thickness of Ibuprofen tablets**

FORMULATION CODE	THICKNESS (mm)		
	UNCOATED*	COATED*	COATING MEMBRANE*
F <sub>1</sub>	3.06±0.04	4.85±0.05	1.79±0.04
F <sub>2</sub>	3.08±0.03	4.84±0.05	1.76±0.04
F <sub>3</sub>	3.06±0.05	4.95±0.04	1.89±0.07
F <sub>4</sub>	3.09±0.06	4.87±0.07	1.78±0.03
F <sub>5</sub>	3.07±0.07	4.81±0.06	1.74±0.05
F <sub>6</sub>	3.20±0.05	4.83±0.03	1.63±0.06

\*All values are expressed as mean  $\pm$  standard deviation, n=3

**Table 4. Hardness and Friability of Ibuprofen tablets**

FORMULATION CODE	HARDNESS (kg/cm <sup>2</sup> )*		FRIABILITY (%)*
	UNCOATED	COATED	UNCOATED
F <sub>1</sub>	5.6±0.52	6.5±0.45	0.09±0.14
F <sub>2</sub>	5.5±0.37	6.3±0.37	0.05±0.15
F <sub>3</sub>	5.2±0.41	6.5±0.60	0.07±0.18
F <sub>4</sub>	5.1±0.58	6.4±0.54	0.05±0.11
F <sub>5</sub>	5.3±0.26	6.3±0.42	0.06±0.20
F <sub>6</sub>	5.2±0.32	6.2±0.28	0.04±0.15

\*All values are expressed as mean  $\pm$  standard deviation, n=3

**Table 5. Weight Variation Test for Coated and Uncoated Ibuprofen Tablets**

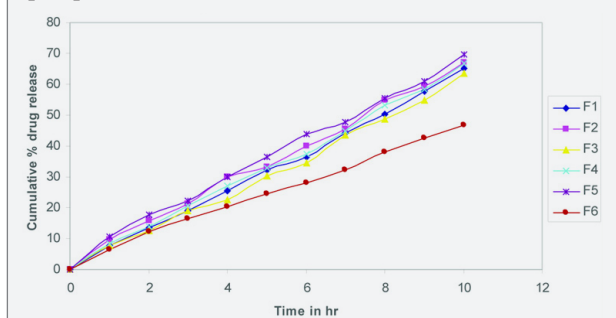
FORMULATION CODE	WEIGHT VARIATION (MG)		WEIGHT GAIN (MG)*	PERCENTAGE WEIGHT GAIN (%)
	UNCOATED*	COATED*		
F <sub>1</sub>	497.62±0.23	516.63±0.14	19.01±0.21	3.852
F <sub>2</sub>	499.52±0.38	516.53±0.28	17.01±0.33	3.405
F <sub>3</sub>	496.51±0.26	517.52±0.32	21.01±0.28	4.232
F <sub>4</sub>	497.50±0.32	515.51±0.23	18.01±0.25	3.664
F <sub>5</sub>	498.52±0.40	515.53±0.45	17.01±0.39	3.412
F <sub>6</sub>	498.52±0.16	514.52±0.34	16±0.32	3.209

\*All values are expressed as mean  $\pm$  standard deviation, n=3

**Table 6. Drug Content of Ibuprofen tablets**

FORMULATION CODE	DRUG CONTENT (%)*	
	UNCOATED	COATED
F <sub>1</sub>	97.60±0.36	97.67±0.34
F <sub>2</sub>	96.60±0.29	96.53±0.23
F <sub>3</sub>	98.33±0.33	98.79±0.19
F <sub>4</sub>	96.11±0.23	96.32±0.25
F <sub>5</sub>	98.72±0.25	98.68±0.45
F <sub>6</sub>	97.05±0.37	97.09±0.23

\*All values are expressed as mean  $\pm$  standard deviation, n=3

**Figure 1. In vitro release profiles of Ibuprofen osmotic pump tablets**

the core materials and osmotic pressure difference between the core contents and the external environment (dissolution medium). Formulation F<sub>6</sub> (control) showed 46.77 % drug release in ten hours. A slower drug release was observed in formulation F<sub>6</sub> (control). This slower drug release may be due to low membrane permeability and increased plasticity of the membrane without osmogens. When comparing all the formulations, F<sub>3</sub> showed a controlled drug release of 63.54% at the end of 10<sup>th</sup> hour. The *in vitro* release profiles

of Ibuprofen osmotic pump tablets were presented in Figure 1.

In order to understand the mechanism of drug release from the formulations, the *in vitro* drug release data were fitted to zero order, first order, Higuchi's model, and Korsmeyer-Peppas equation. When the data were plotted according to zero order, the formulations showed a high linearity, with regression co-efficient values (R<sup>2</sup>) between 0.9971-0.9992 indicating that the drug release was according to the Zero order kinetics. The R<sup>2</sup> values of zero order kinetics for Formulation F<sub>1</sub>, F<sub>2</sub>, F<sub>3</sub>, F<sub>4</sub> and F<sub>5</sub> were 0.9975, 0.9987, 0.9971, 0.9983 and 0.9992 respectively and found to be greater than R<sup>2</sup> values of first order, Higuchi's model, and Korsmeyer-Peppas equation indicating that the drug release was according to the Zero order kinetics. The results of all formulations showed 'n' values more than 0.5 and formulations F<sub>2</sub>, F<sub>4</sub> showed behaviour of Non - Fickian transport mechanism and formulations F<sub>1</sub>, F<sub>3</sub> and F<sub>5</sub> showed behaviour of Super case II transport mechanism. The release rate kinetic data for all the formulations are shown in Table 7.

**Table 7. Kinetic data of Ibuprofen formulations**

FORMULATION CODE	ZERO ORDER	FIRST ORDER	HIGUCHI	KORSMEYER -PEPPAS		
	REGRESSION COEFFICIENT (r <sup>2</sup> )				n	
F <sub>1</sub>	0.9975	0.9814	0.9282	0.9958	0.9229	
F <sub>2</sub>	0.9987	0.9841	0.9408	0.9980	0.8740	
F <sub>3</sub>	0.9971	0.9767	0.9210	0.9956	0.9462	
F <sub>4</sub>	0.9983	0.9806	0.9319	0.9969	0.8665	
F <sub>5</sub>	0.9992	0.9859	0.9485	0.9997	0.9726	

**Table 8. Stability study data of Formulation F3**

TEMPERATURE	DRUG CONTENT (%)*			CUMULATIVE PERCENTAGE DRUG RELEASE AT THE END OF 10 HR (%)*		
	31 <sup>st</sup> DAY	46 <sup>th</sup> DAY	61 <sup>st</sup> DAY	31 <sup>st</sup> DAY	46 <sup>th</sup> DAY	61 <sup>st</sup> DAY
27 <sup>o</sup> ±2 <sup>o</sup> C/60 ± 5% RH	98.11±0.24	97.29±0.39	97.94±0.59	64.64±0.25	64.41±0.49	64.34±0.48
50 <sup>o</sup> ±2 <sup>o</sup> C/75 ± 5% RH	97.76±0.20	97.34±0.55	98.45±0.63	63.43±0.62	64.07±0.14	64.23±0.45

\*All values are expressed as mean ± standard deviation, n=3

Based on controlled drug release formulation F<sub>3</sub> was selected and subjected for stability study by storing at 27<sup>o</sup>±2<sup>o</sup>C/60 ± 5% RH and 50<sup>o</sup>±2<sup>o</sup>C/75 ± 5% RH for 60 days. After 60 days of storage, the formulation was observed physically and there was no colour change. The samples were analyzed for drug content and dissolution studies at intervals of 31<sup>st</sup>, 46<sup>th</sup> and 61<sup>st</sup> days. The stability study results showed that percentage of Ibuprofen content was between 97.29 % and 98.45 %. It revealed that there was no degradation of Ibuprofen in formulation F<sub>3</sub>. Also it was observed that there was no significant change in the release rate of Ibuprofen from formulation F<sub>3</sub> after 60 days. These results indicated that the formulation F<sub>3</sub> was stable even after storing at 27<sup>o</sup>±2<sup>o</sup>C/60 ± 5% RH and 50<sup>o</sup>±2<sup>o</sup>C/75 ± 5% RH for 60 days. The results are presented in Table 8.

## CONCLUSION

From the above study, it was concluded that Ibuprofen osmotic pump tablet prepared with potassium chloride (10%) as osmogen and cellulose acetate as coating polymer has control the release of drug for 10 hours. The stability study of the formulation F<sub>3</sub> carried out by storing at 27<sup>o</sup>±2<sup>o</sup>C and 50<sup>o</sup>±2<sup>o</sup>C for 60 days showed that there was no significant change in the drug content and percentage drug release. It proved that the product was stable. Hence this formulation may be considered as a suitable alternative to currently available formulations of Ibuprofen.

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